

# Ethyl 4-hydroxy-2,6-diphenyl-5-(phenylsulfanyl)pyridine-3-carboxylate and ethyl 2,6-bis(4-fluorophenyl)-4-hydroxy-5-(4-methylphenylsulfanyl)pyridine-3-carboxylate: supramolecular aggregation through C—H...O, C—H...F and C—H... $\pi$ interactions

J. Suresh,<sup>a</sup> R. Suresh Kumar,<sup>b</sup> S. Perumal,<sup>b</sup> A. Mostad<sup>c</sup> and S. Natarajan<sup>d\*</sup>

<sup>a</sup>Department of Physics, The Madura College, Madurai 625 011, India, <sup>b</sup>School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India, <sup>c</sup>Department of Chemistry, University of Oslo, PO Box 1033, Blindern, N-0315 Oslo 3, Norway, and <sup>d</sup>Department of Physics, Madurai Kamaraj University, Madurai 625 021, India  
Correspondence e-mail: s\_natarajan50@yahoo.com

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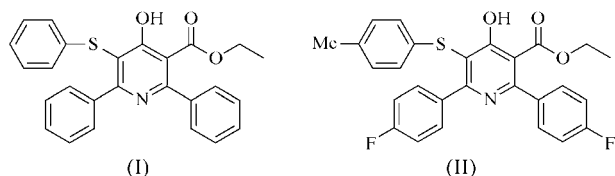
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The title polysubstituted pyridines, ethyl 4-hydroxy-2,6-diphenyl-5-(phenylsulfanyl)pyridine-3-carboxylate,  $C_{26}H_{21}NO_3S$ , (I), and ethyl 2,6-bis(4-fluorophenyl)-4-hydroxy-5-(4-methylphenylsulfanyl)pyridine-3-carboxylate,  $C_{27}H_{21}F_2NO_3S$ , (II), adopt nearly planar structures. The crystal structure of (I) is stabilized by intermolecular C—H...O and C—H... $\pi$  interactions. The C—H...O hydrogen bonds generate rings of motifs  $R_2^2(14)$  and  $R_2^2(20)$ . The crystal structure of (II) is stabilized by intermolecular C—H...F and C—H... $\pi$  interactions. The C—H...F bond generates a linear chain of motif  $C(14)$ . In addition, in (I) and (II), intramolecular O—H...O interactions generating a graph-set motif  $S(6)$  are found. No significant aryl-aryl or  $\pi$ - $\pi$  interactions exist in these structures.

## Comment

Pyridines are of great interest because of the occurrence of their saturated and partially saturated derivatives in biologically active compounds and natural products such as NAD



nucleotides, pyridoxol (vitamin B6) and pyridine alkaloids (Balasubramanian & Keay, 1996). Substituted pyridines have

also found a number of applications, *viz.* as anticorrosion agents, insecticides and as potential drug substances (Keney, 1968; Goodhue, 1967; Cooke *et al.*, 1998). In this context, the synthesis of polysubstituted pyridines has been an active research area for many years in our laboratory. The present work reports the X-ray crystallographic study of two such substituted pyridines, *viz.* (I) and (II) (see scheme).

The molecular structures of (I) and (II) are shown in Figs. 1 and 2, respectively, and selected geometric parameters are given in Tables 1 and 3, respectively. In (I) and (II), the pyridine heterocycles are planar; the displacements of the atoms from their mean planes do not exceed 0.043 (2) Å. None of the substituted groups forming a plane is either

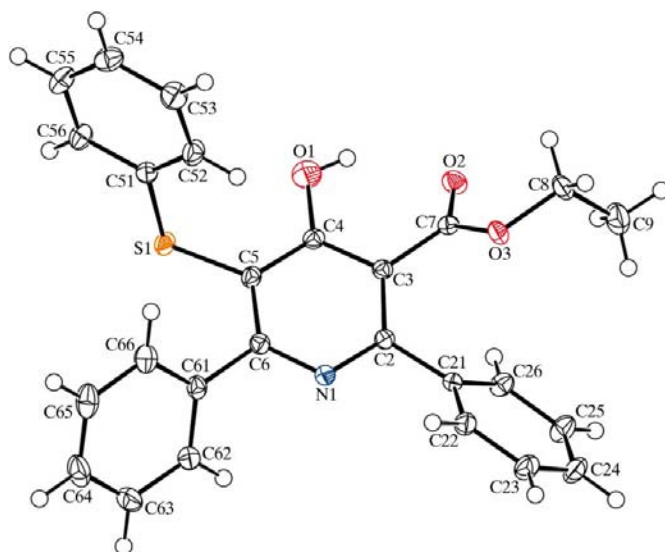


Figure 1

The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are represented as small spheres of arbitrary radii.

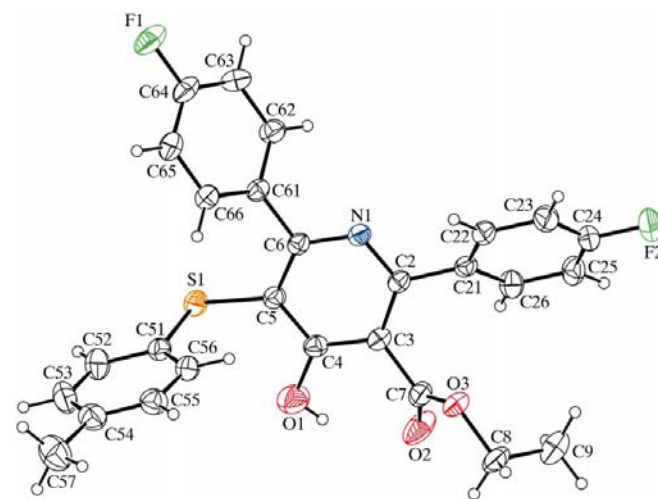


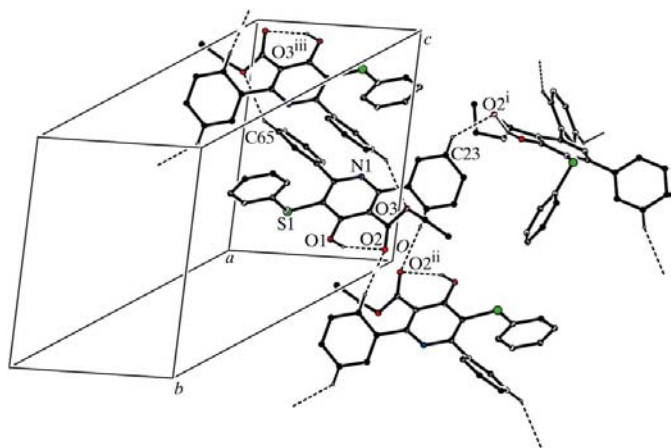
Figure 2

The molecular structure of (II), showing 30% probability displacement ellipsoids and the atom-numbering scheme. H atoms are represented as small spheres of arbitrary radii.

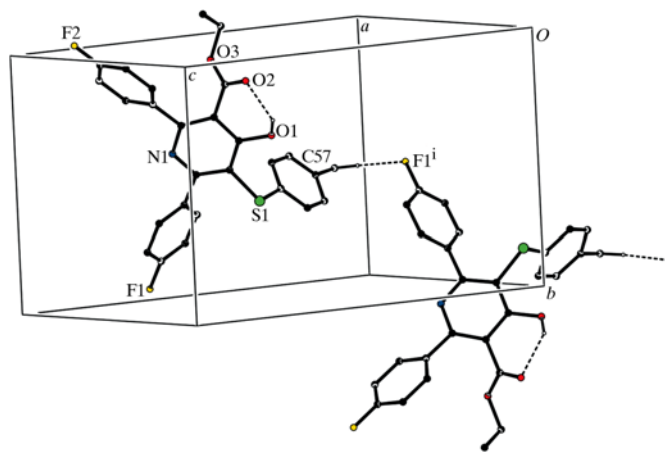
coplanar with or orthogonal to the pyridine ring. The dihedral angles of the phenylsulfanyl group at C5, the ethoxycarbonyl group at C3 and the benzene ring at C2 with the pyridine ring are 76.2, 37.8 and 43.7°, respectively, in (I), and 83.6 (1), 46.4 (1) and 39.2 (1)°, respectively, in (II). The phenylsulfanyl group is *cis* to the benzene ring at C6, with dihedral angles of 62.6 (1)° in (I) and 70.5 (2)° in (II). The C5—S1 bond [1.769 Å in (I) and 1.770 Å in (II)] is slightly shorter than the C51—S1 bond [1.782 Å in (I) and 1.778 Å in (II)], which may be due to the conjugation of atom S1 with the pyridine ring. Similarly, the C7—O3 bond [1.335 Å in (I) and 1.332 Å in (II)] is longer

than the C7—O2 bond [1.222 Å in (I) and 1.203 Å in (II)] and considerably shorter than C8—O3 [1.462 Å in (I) and 1.468 Å in (II)], which demonstrates the conjugation of atom O3 with C7—O2.

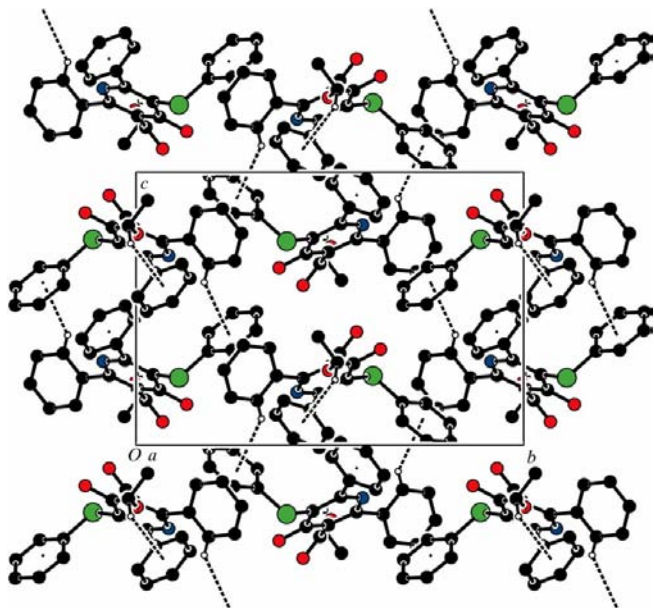
The crystal structure of (I) is stabilized by weak C—H···O interactions. The C26—H26···O2 and C65—H65···O3 interactions form cyclic dimers, generating rings of graph-set motifs  $R_2^2(14)$  and  $R_2^2(20)$ , respectively (Etter *et al.*, 1990) (Table 2 and Fig. 3). The intramolecular hydrogen bond found between the hydroxyl and carboxylate groups (O1—H1···O2) (Table 2 and Fig. 3) generates a graph-set motif  $S(6)$ . Two weak C—H··· $\pi$  interactions, *viz.* C22—H22···Cg1<sup>i</sup> and C8—H8B···Cg2<sup>ii</sup> (Cg1 and Cg2 are the centroids of rings C51—C56 and C61—C66, respectively; symmetry codes are given in Table 2) are observed. No  $\pi$ — $\pi$  interactions or significant aryl—aryl inter-



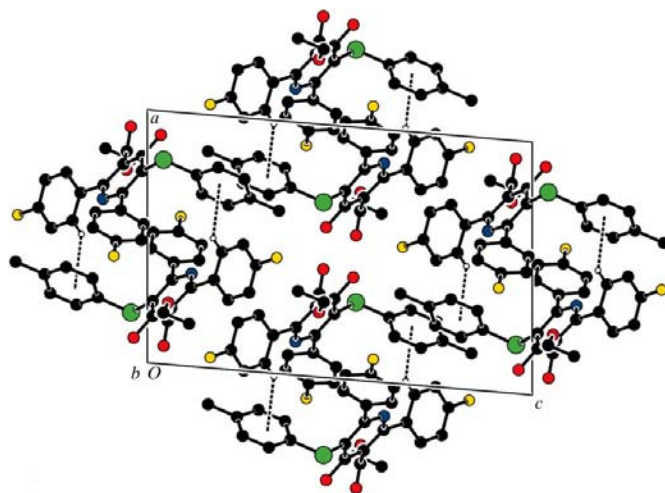
**Figure 3**  
A partial packing view, showing the intermolecular C—H···O hydrogen bonding (dashed lines) in compound (I). H atoms are shown as small spheres of arbitrary radii. H atoms not involved in hydrogen-bonding interactions have been omitted for clarity. [Symmetry codes: (i)  $-x, y - \frac{1}{2}, \frac{1}{2} - z$ ; (ii)  $-x, -y, -z$ ; (iii)  $1 - x, -y, 1 - z$ .]



**Figure 5**  
A partial packing view, showing the intermolecular C—H···F hydrogen bonding (dashed lines) in compound (II). H atoms are shown as small spheres of arbitrary radii. H atoms not involved in hydrogen-bonding interactions have been omitted for clarity. [Symmetry codes: (i)  $x - \frac{1}{2}, -y + \frac{3}{2}, z - \frac{1}{2}$ .]



**Figure 4**  
The packing of the molecules of (I), showing the C—H··· $\pi$  interactions (dashed lines) within the unit cell, viewed down the *a* axis. H atoms are shown as small spheres of arbitrary radii. H atoms not involved in hydrogen-bonding interactions have been omitted for clarity.



**Figure 6**  
The packing of the molecules of (II), showing the C—H··· $\pi$  interactions (dashed lines) within the unit cell, viewed down the *b* axis. H atoms are shown as small spheres of arbitrary radii. H atoms not involved in hydrogen-bonding interactions have been omitted for clarity.

actions are observed. The molecular packing in the unit cell is shown in Fig. 4.

The crystal structure of (II) is stabilized by a weak C—H...F interaction. This C57—H57C...F1 interaction (Table 4 and Fig. 5) forms a linear chain generating a *C*(14) graph-set motif. An intramolecular hydrogen bond found between the hydroxyl and carboxylate groups (O1—H1...O2) (Table 4 and Fig. 5) generates an *S*(6) graph-set motif. The supramolecular aggregation is completed by the presence of a weak C—H... $\pi$  interaction (Table 4). The molecular packing in the unit cell is shown in Fig. 6. The geometry of the C—H... $\pi$  interaction was obtained from *PLATON* (Spek, 2003)

## Experimental

For the preparation of (I), dichlorodicyanobenzoquinone (DDQ-H2; 0.105 g, 0.4 mmol) was added to a solution of ethyl 4-hydroxy-2,6-diphenyl-5-(phenylsulfanyl)-1,2,5,6-tetrahydropyridine-3-carboxylate (0.1 g, 0.2 mmol) in benzene (10 ml), and the mixture was refluxed in a water bath for 30 min. The precipitated DDQ-H2 was filtered off and the filtrate evaporated under vacuum. The residue was recrystallized from ethanol to give (I) (yield 0.072 g, 73%; m.p. 421–422 K). For the preparation of (II), DDQ-H2 (0.094 g, 0.4 mmol) was added to a solution of ethyl 2,6-bis(4-fluorophenyl)-4-hydroxy-5-[4-methylphenylsulfanyl]-1,2,5,6-tetrahydropyridine-3-carboxylate (0.1 g, 0.2 mmol) in benzene (10 ml), and the mixture was refluxed in a water bath for 30 min. The precipitated DDQ-H2 was filtered off and the filtrate evaporated under vacuum. The residue was recrystallized from ethanol to give (II) (yield 0.071 g, 72%; m.p. 380–381 K).

## Compound (I)

### Crystal data

$C_{26}H_{21}NO_3S$	$Z = 4$
$M_r = 427.50$	$D_x = 1.325 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 10.3728$ (2) Å	$\mu = 0.18 \text{ mm}^{-1}$
$b = 17.1008$ (4) Å	$T = 105$ (2) K
$c = 12.9444$ (3) Å	Block, colourless
$\beta = 111.041$ (1)°	$0.28 \times 0.14 \times 0.12 \text{ mm}$
$V = 2143.02$ (8) Å <sup>3</sup>	

### Data collection

Bruker SMART APEX CCD area-detector diffractometer	32101 measured reflections
$\omega$ scans	5325 independent reflections
Absorption correction: multi-scan ( <i>SADABS</i> ; Bruker, 1998)	4855 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.97$ , $T_{\max} = 0.979$	$R_{\text{int}} = 0.043$
	$\theta_{\text{max}} = 28.3^\circ$

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0504P)^2 + 1.7947P]$
$R[F^2 > 2\sigma(F^2)] = 0.040$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.112$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 1.02$	$\Delta\rho_{\text{max}} = 0.84 \text{ e } \text{Å}^{-3}$
5325 reflections	$\Delta\rho_{\text{min}} = -0.78 \text{ e } \text{Å}^{-3}$
280 parameters	
H-atom parameters constrained	

**Table 1**

Selected bond lengths (Å) for (I).

S1—C5	1.7693 (13)	O3—C8	1.4622 (16)
S1—C51	1.7819 (14)	O2—C7	1.2216 (16)
O3—C7	1.3350 (16)		

**Table 2**

Hydrogen-bond geometry (Å, °) for (I).

$Cg1$  and  $Cg1'$  are the centroids of rings C51–C56 and C61–C66, respectively.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1...O2	0.82	2.04	2.7450 (16)	144
C23—H23...O2 <sup>i</sup>	0.93	2.59	3.3168 (18)	136
C26—H26...O2 <sup>ii</sup>	0.93	2.46	3.3446 (17)	158
C65—H65...O3 <sup>iii</sup>	0.93	2.59	3.4008 (18)	146
C22—H22... $Cg1$ <sup>iii</sup>	0.93	2.89	3.6647 (15)	142
C8—H8B... $Cg2$ <sup>iv</sup>	0.97	2.75	3.6458 (16)	154

Symmetry codes: (i)  $-x, y - \frac{1}{2}, -z + \frac{3}{2}$ ; (ii)  $-x, -y, -z$ ; (iii)  $-x + 1, -y, -z + 1$ ; (iv)  $x + 1, y, z$ .

## Compound (II)

### Crystal data

$C_{27}H_{21}F_2NO_3S$	$Z = 4$
$M_r = 477.52$	$D_x = 1.357 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 12.092$ (1) Å	$\mu = 0.18 \text{ mm}^{-1}$
$b = 10.489$ (1) Å	$T = 293$ (2) K
$c = 18.496$ (2) Å	Block, colourless
$\beta = 94.78$ (1)°	$0.18 \times 0.16 \times 0.12 \text{ mm}$
$V = 2337.7$ (4) Å <sup>3</sup>	

### Data collection

Nonius MACH3 four-circle diffractometer	4099 independent reflections
$\omega$ scans	2764 reflections with $I > 2\sigma(I)$
Absorption correction: $\psi$ scan (North <i>et al.</i> , 1968)	$R_{\text{int}} = 0.020$
$T_{\min} = 0.992$ , $T_{\max} = 0.995$	$\theta_{\text{max}} = 25.0^\circ$
4815 measured reflections	3 standard reflections
	frequency: 60 min
	intensity decay: none

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0654P)^2 + 0.8462P]$
$R[F^2 > 2\sigma(F^2)] = 0.043$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.128$	$(\Delta/\sigma)_{\text{max}} = 0.011$
$S = 1.01$	$\Delta\rho_{\text{max}} = 0.34 \text{ e } \text{Å}^{-3}$
4097 reflections	$\Delta\rho_{\text{min}} = -0.41 \text{ e } \text{Å}^{-3}$
310 parameters	
H-atom parameters constrained	

**Table 3**

Selected bond lengths (Å) for (II).

S1—C5	1.770 (2)	O3—C7	1.322 (3)
S1—C51	1.778 (3)	O3—C8	1.468 (3)
O2—C7	1.203 (3)		

**Table 4**

Hydrogen-bond geometry (Å, °) for (II).

$Cg1$  is the centroid of the C51–C56 ring.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1...O2	0.82	2.09	2.782 (3)	142
C57—H57C...F1 <sup>i</sup>	0.96	2.51	3.393 (4)	153
C22—H22... $Cg1$ <sup>ii</sup>	0.93	2.97	3.749 (3)	143

Symmetry codes: (i)  $x - \frac{1}{2}, -y + \frac{3}{2}, z - \frac{1}{2}$ ; (ii)  $-x + 2, -y + 1, -z + 1$ .

H atoms were placed in calculated positions and allowed to ride on their carrier atoms, with C—H = 0.93–0.97 Å and O—H = 0.82 Å, and with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  for CH<sub>2</sub> and CH groups,  $1.5U_{\text{eq}}$  for CH<sub>3</sub> groups and  $1.5U_{\text{eq}}(\text{O})$  for OH groups.

Data collection: *SMART* (Bruker, 2001) for (I); *CAD-4 EXPRESS* (Enraf–Nonius, 1994) for (II). Cell refinement: *SAINT* (Bruker, 2001) for (I); *CAD-4 EXPRESS* for (II). Data reduction: *SAINT* for (I); *XCAD4* (Harms & Wocadlo, 1996) for (II). For both compounds, program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DN3034). Services for accessing these data are described at the back of the journal.

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